Methyl Bromide

H_3C-Br

74-83-9

I. Physical and Chemical Properties

Description	Colorless gas
Molecular formula	CH_3Br
Molecular weight	94.95
Air concentration conversion	1 ppm = 3.89 mg/m^3 @ 25°C

II. Overview

Some evidence of teratogenicity and reduced birth weight has been observed after methyl bromide exposure in rabbits and rats. Developmental toxicity is a key toxicological endpoint of concern for infants and children. Damage sustained following prenatal exposure poses health concerns postnatally, and, thus should be considered in evaluating impacts on infants and children. Neurotoxicity due to methyl bromide (MeBr) exposure has been reported in occupational settings, accidental exposures, and in animal studies. Neurotoxicity is also an endpoint of concern for infants and children, primarily due to the prolonged period of development of the nervous system (e.g., through adolescence). However, exposures to MeBr from non-agricultural stationary sources are not widespread. Therefore, MeBr was proposed for listing in Tier 2 in the initial prioritization of TACs (see Table 1 of the Introduction).

III. Principal Sources of Exposure

Current uses of MeBr include the fumigation of homes and other structures for termites and other pests. Methyl bromide is also used to fumigate soil before planting, and fruits and vegetables after harvest. In 1981, 6.3 million pounds of MeBr were reported to have been used in California (Alexeeff and Kilgore, 1983). In 1991, its use had grown to 18.7 million pounds in the state (Cal/EPA, 1993). It should be noted that only stationary source emissions of methyl bromide can be regulated by the Air Resources Board and the local air districts. No data were available to characterize the quantity of methyl bromide emissions from such sources.

IV. Potential for Differential Effects

A. Summary of Key Human Studies

Methyl bromide is neurotoxic in both humans and animals. Neurotoxicity is one of the key toxicological endpoints for infants and children. Human studies reporting neurotoxicity are described in the following paragraphs.

During a two-week manufacturing operation, 90 persons were exposed to concentrations of MeBr generally less than 35 ppm (136 mg/m^3) (Watrous, 1942). Symptoms of toxicity developed sometime during the workshift, for example, following a few hours of exposure. In others, the symptoms were delayed and did not develop until several hours following the shift. The symptoms occurred in 33 of the 90 workers and were described as mild systemic symptoms primarily of anorexia, nausea and headache. Anorexia (reported by 25 of the 90 workers) was a common symptom and in some cases lasted for a week or more post-exposure, but without marked weight-loss. In some cases, the symptoms progressed to vomiting. Headache was a fairly common symptom (16 of 90) which disappeared when exposure ceased. While exposure was measured in a crude fashion using a "Frigidaire Leak Detector" (measures halides by color of flame), extensive monitoring was conducted throughout the manufacturing operation. In general, concentrations were at or below the limit of detection of 35 ppm.

Workers (n = 32) exposed to MeBr during fumigation of soil or structures were compared to a referent group of 29 workers not exposed to MeBr, but exposed to other fumigants (Anger *et al.*, 1986). Exposures to MeBr were not quantified. It was found that workers exposed to MeBr had a higher rate of neurological symptoms and performed less well on several behavioral tests. Several confounding factors were present in this study, including lack of adjustments for age, alcohol consumption, prescription medication, illegal drugs, education, or ethnic group between the exposed and the referent groups.

Nine Dutch greenhouse workers were exposed to methyl bromide from an adjacent fumigated area via poor seals around a door and open pipes (Hustinx *et al*., 1993). Methyl bromide used (200 g/m^3) was 5 times the legal amount. Some workers had been previously exposed to methyl bromide and had experienced symptoms (nausea, vomiting, dizziness, and poor memory). On the first day of fumigation, the methyl bromide level was 25 ppm in the nonfumigated side. On the second day when the workers were poisoned, the methyl bromide levels ranged from 150 to 200 ppm. All, except one worker, experienced extreme nausea, repeated vomiting, and dizziness. The other one felt only a burning sensation in the throat. Two workers later developed seizures. Others complained of headache, nausea, ataxia, slurred speech, and a sensation described as "floating." The serum bromide levels ranged from 51 to 363 mg/L. Most of the workers serum bromide levels (5-119 mg/L) remained elevated 19 days after exposure. The severity of the symptoms did not correlate with the bromide levels, but was associated with known previous exposures to methyl bromide.

A study by Garnier *et al*. (1996) found that two workers similarly exposed to high concentrations of MeBr (about 17,000 mg/m^3) exhibited substantially different symptoms. Glutathione-S-transferase (GST) activity was measured in the erythrocytes of both patients. GST activity was apparent in the patient with severe poisoning who was, therefore, considered a conjugator. The second patient who exhibited only mild symptoms lacked measurable GST activity in the erythrocytes and was therefore classed as a nonconjugator. Conjugators appear to be homozygous or heterozygous bearers of the gene for GST, which is not restircted to the erythrocytes. As cited by Garnier *et al*. (1996), the gene is lacking in 20.4 % of whites, 21.8% of African-Americans, 64.6% of Chinese-Americans, 60.2% of Korean-Americans, and 9.7% of Mexican-Americans. Thus, conjugation of MeBr with glutathione may be a toxifying step for neurotoxicity and the ability to conjugate may reflect susceptibility to neurotoxicity. However, conjugation apparently protects against the cytogenetic effects of MeBr (Hallier *et al*., 1993). These latter investigators note that about one-quarter of the human population does not possess GST activity in erythrocytes, and that this enzyme is not found in erythrocytes of laboratory animals (rats and mice). For this reason, studies in laboratory rodents may underestimate the neurotoxicity of MeBr in humans.

B. Summary of Key Animal Studies

A number of studies have demonstrated that methyl bromide is neurotoxic in animals. Although studies that evaluated differential effects in immature and mature animals are not available, neurotoxicants are a general concern because the nervous system develops over a prolonged period of time into adolescence. Neurotoxic effects observed in several studies are summarized below.

Kato *et al*. (1986) observed focal lesions in the brain in rats (10-12 per group) after inhalation of 150 ppm (585 mg/m^3) MeBr 4 hours/day, 5 days/week for 11 weeks. In another experiment, rats were exposed to 0, 200, 300, or 400 ppm (0, 777, 1160, or 1550 mg/m^3) MeBr 4 hours/day, 5 days/week for 6 weeks. Exposures of 300 ppm or greater resulted in neurological dysfunction, including ataxia and paralysis.

Anger *et al*. (1981) determined that rabbits are more sensitive than rats to MeBr-induced neurotoxicity. In this study, rats or rabbits were exposed to 0 or 65 ppm (0 or 254 mg/m^3) MeBr for 7.5 hours/day, 4 days/week, for 4 weeks. Nerve conduction velocity and eyeblink reflex were impaired in rabbits but not rats exposed to 65 ppm MeBr. Similarly, rats did not exhibit neurological signs after exposure to 55 ppm (215 mg/m^3) MeBr for 36 weeks. Rabbits exposed to 26.6 ppm (104 mg/m^3) 7.5 hr/day, 25 total hours per week for 30 weeks did not display any neurological effects (Russo *et al.*, 1984).

The National Toxicology Program (NTP) conducted 14-day, 6-week, 13-week and 103 week wxposures to study the toxicology and carcinogenesis of MeBr in rats and mice (NTP, 1992). Neurotoxic effects were noted in all the studies. In the 14-day study, groups of fove B6C3F1 mice of each sex were exposed via inhalation to 0, 12, 25, 50, 100, or 200 ppm MeBr 6 hours/day, 5 days/week for 2 weeks. All MeBr exposed groups exhibited signs of neurotoxicity including trembling, jumpiness, and paralysis, which were more pronounced and severe in the animals exposed to 50 ppm and higher. In the 6-week study, rats and mice (5 animals/sex/group) were exposed to 0 or 160 ppm (0

or 624 mg/m^3). Animals in the 160 ppm dose group showed high mortality rates, loss in body weight and histological changes in multiple organ systems including brain, kidney, nasal cavity, heart, adrenal gland, liver, and testes (NTP, 1992). Brain lesions included necrosis in the thalamus, hippocampus, and cerebellum.

In the 13-week study, 18 rats/sex/group were exposed to 0, 30, 60, or 120 ppm (0, 117, 233, or 466 mg/m^3) MeBr for 6 hours/day, 5 days/week. The mice were exposed to 0, 10, 20, 40, 80, or 120 ppm (0, 39, 78, 155, 311, or 466 mg/m^3) 6 hours/day, 5 days/week. Pseudocholinesterase activity and neurobehavioral tests were conducted in the mice. Serious effects, including 58% body weight loss, 17% mortality and severe curling and crossing of the hindlimbs were observed in mice exposed to 120 ppm MeBr. There were no changes in pseudocholinesterase activity.

A carcinogenesis bioassay was also conducted by NTP. Mice (86 animals/group) were exposed to 0, 10, 33, or 100 ppm (0, 38.8, 128, or 388 mg/m^3) MeBr for 6 hours/day, 5 days/week, for 103 weeks (NTP, 1992). In this study, high mortality rates in both males and females in the 100 ppm group resulted in a discontinuation of exposure after 20 weeks. A low incidence of sternal dysplasia and a significant decrease in locomotor activity at some time points (but not other later time points) were noted in the 10 ppm group. No differences were consistently observed in neurobehavioral tests between controls and the 10 or 33 ppm dose groups. Statistically significant quantitative behavioral changes were noted in the high dose males at 3 months. The animals had a heightened response to sound compared to controls and were less active than controls. Hindlimb grip was impaired in the high-dose male mice, and they showed a longer latency than controls in the hot plate test. After 6 months, female mice in the 100 ppm group were significantly less active than controls but their previous heightened response to startle had disappeared. At 9 months, there were no differences between treatment group females, but when tested at 24 months, lower activity and heightened startle response were again apparent in the 100 ppm females. Treatment-related cerebellar and cerebral degeneration was observed in the high-dose males and females. The authors note that degenerative changes in the cerebellum and cerebrum were noted more often in animals that died early possibly indicating an association between these toxic effects and mortality.

Neurotoxicity was also noted in other studies of short-term exposures. A 5-day exposure of rats (10 animals/group) to 0, 90, 175, 250, or 325 ppm (0, 350, 680, 971, or 1260 mg/m^3) resulted in lesions in the nasal olfactory sensory cells, and the cerebellum beginning at 175 ppm (Hurtt *et al.*, 1987). Hurtt and Working (1988) later observed severe histological damage to the nasal epithelium following a single exposure to 90 or 200 ppm (351 or 780 mg/m^3) MeBr. Olfactory function, measured by the ability to locate buried food, was impaired at the 200 ppm exposure.

Sikov *et al.* (1981) in evaluating the teratogenic potential of MeBr in rats and rabbits exposed to 0, 20, or 70 ppm (0, 78, or 272 mg/m^3) 7 hours/day, 5 days/week for 3 weeks during days 1-19 (rats) or 1-24 (rabbits) of gestation, noted no maternal or fetal effects in the rats; however, severe maternal neurotoxic effects were observed in the rabbits that resulted in 24/25 deaths. In this study, no significant maternal or fetal effects were observed at a concentration of 20 ppm.

Methyl bromide exposure is associated with developmental toxicity in some animal studies. Developmental toxicity is a key toxicological endpoint for infants and children. As discussed in the Introduction to the report, fetal damage sustained as a result of exposure to toxicants is a source of adverse health impacts postnatally, and therefore falls within the scope of this report.

MeBr (99.9% pure) was administered to Sprague Dawley rats of both sexes by whole-body inhalation 6 hours per day and 5 days per week at the nominal concentrations of 0, 3, 30, or 90 ppm (American Biogenics Corp., 1986; Hardisty, 1992; Busey, 1993). Parental animals were exposed for about 40 or 55 days and 90 to 105 days before their first and second matings, respectively, and were exposed for a total of 132-145 days before they were sacrificed. There was no exposure to MeBr between gestation day 21 and lactation day 4 in any of the four birthing periods. The pups were not directly exposed to MeBr until after weaning (postnatal day 28). Body weights (91-95% of control values) and body weight gain (76% of control values) during the pre-mating periods were significantly decreased only in the F_0 males of the 90 ppm group. For the 30 and 90 ppm F_1 groups, the body weights at pre-mating and during reproduction were consistently lower than those of controls. The absolute brain (wet) weights of the F_0 males, F_1 males, and F_1 females in the 90 ppm groups were significantly ($p > 0.05$) decreased by 5%, 6%, and 6%, respectively, compared with controls. The brain weight of the F_1 females of the 30 ppm group was also reduced by 5% ($p > 0.05$). These findings are interesting in light of the known neurotoxic effects observed in mature animals.

At birth, the pup body weights of the treated groups were either higher or not significantly different from controls; the only exception was the lowered body weight of the F_{2a} 90 ppm group. During lactation, the F_{1a} and F_{1b} pups of the 30 and 90 ppm groups showed significantly reduced body weights on lactation days 14 to 28. The F_{2a} 90 ppm pup body weights were lower at birth than the controls and remained reduced throughout lactation. The F_{2a} 30 ppm pup body weights showed significant reduction on lactation days 14 to 28. The F_{2b} 30 and 90 ppm pup body weights were decreased, starting as early as 4 days after birth. The reduction in body weight was greater in the F_{2a} and F_{2b} progeny (reduction of 9 to 21 % at 90 ppm) compared respectively to the F_{1a} and F_{1b} pups (reduction of 5 to 11 % at 90 ppm). Since the pups were not exposed to MeBr during the lactation period, except perhaps via the maternal milk, the finding of reduced body weights suggested that growth retardation might be an effect due to the 14 to 15 days of *in utero* exposure.

For the female F_{2b} progeny from the 90 ppm group, the absolute weights of the brain, heart, kidneys, and liver were reduced significantly ($p \leq 0.05$) by 7%, 15%, 18%, and 23% when compared to control values, respectively. The absolute weights of the kidneys, liver, and testes of the corresponding male progeny were also reduced, though to a lesser degree. The organ to body weight ratios were generally not significantly different from control values.

Histology data showed a decrease in the width of the cerebral cortex of the F_1 90 ppm groups (both sexes), which can be construed as developmental neurotoxicity. The reduced brain (fixed) weights for the F_1 30 ppm females suggested that the LOAEL for the reduced cerebral-cortex width was 30 ppm. Quantitative histological parameters were not affected in the F_0 90 ppm adults which suggested that the effects in the F_1 animals were the result of *in utero* and/or lactational exposure.

The parental NOAEL was 3 ppm based on reduced fertility. The progeny NOEL was 3 ppm based on the decreased pup body weights and organ weights, reduced F_1 brain weight and reduced cerebral cortex width at 30 ppm.

Exposure of pregnant New Zealand white rabbits to MeBr at 80 ppm from gestation days 7 to 19 resulted in maternal neurotoxicity and decreased body weight (Breslin *et al*., 1990). Developmental effects observed in the fetuses of the 80 ppm group included omphalocele, retro-esophageal right subclavian artery, gall bladder agenesis, fused sternebrae, and decreased fetal body weight. No effects on the fetuses and does were observed at 40 ppm (155 mg/m^3). The gall bladder agenesis was considered a significant finding due to the very low incidence in historical controls. Thirteen fetuses from 5 does had no gall bladder. Three of the does did not exhibit symptoms of toxicity; the gall bladder agenesis thus occurred at doses lower than those necessary for significant maternal toxicity.

In summary, MeBr has been demonstrated to induce neurotoxicity in adult animals; observed effects include brain and olfactory sensory cell histological lesions, motor and sensory dysfunction. Developmental toxicity endpoints noted include decreased pup body and organ weights and organ and skeletal abnormalities, including reduced cerebral cortex widths. This last effect combined with the neurotoxicity data from adult animals suggests that fetal or neonatal animals may be at increased risk of developmental neurotoxicity from MeBr exposure compared to adult animals.

V. Additional Information

A. Genotoxicity and Carcinogenicity

MeBr is genotoxic in *in vitro* and *in vivo* mutation assays (reviewed by IARC, 1999). It is a direct-acting mutagen in Salmonella mutation assays and the mouse lymphoma L5178Y assay, causes increased micronuclei formation in mouse bone marrow and peripheral blood cells and increased frequencies of sister chromatid exchange (SCE) in CHO cells and in mouse bone marrow cells *in vivo*. DNA alkylation was detected in both rats and mice after *in vivo* exposure by the oral, intraperitoneal, or inhalation routes, and DNA damage was found in the germ cells of rats after inhalation exposure. Occupational studies suggest that MeBr may also be genotoxic to humans. Increased lymphocyte SCE frequencies and blood protein (S-methylcysteine) adducts were observed in soil fumigators (Hallier *et al.*, 1993). Structural fumigation workers have been found to have increased incidences of micronuclei and hypoxanthine-guanine phosphoribosyl transferase (*hprt*) mutations in lymphocytes and oropharyngeal cells (Calvert *et al.*, 1998a,b).

In contrast, MeBr has not been demonstrated to be carcinogenic in animal bioassays. Tumor incidence was not increased in male and female Wistar rats exposed to MeBr by whole-body inhalation at concentrations of 0, 3, 30 or 90 ppm (0, 12, 117 or 350 mg/m^3) for 6 hours/day, five days/week for 29 months (Reuzel *et al.*, 1991). MeBr did not induce significant increases in any tumor types in the 2-year mouse inhalation exposure study described above (NTP, 1992). Gotoh et al. (1984) report no

treatment-related increases in incidence of tumors in male and female BDFI mice exposed to MeBr by whole-body inhalation at concentrations of 0, 4, 16 or 64 ppm (0, 16, 62 or 249 mg/m^3) for 6 hours/day, five days/week for 104 weeks. The incidence of pituitary gland adenomas was significantly increased in male Fischer 344/DuCrj rats (whole body MeBr inhalation exposure at 0, 4, 20 or 100 ppm (0, 16, 78 or 389 mg/m^3) for 6 hours/day, five days/week for 104 weeks) when compared to controls (16/50, 23/50, 19/50 and 30/50 in control, 4, 20 and 100 ppm groups, respectively; $p < 0.01$) (Gotoh *et al.*, 1994). However, no increase in tumor incidence was noted in female rats exposed in the same study to the same MeBr concentrations as the male rats. The IARC and US EPA classifications for MeBr are Group 3 (not classifiable as to its carcinogenicity in humans) (IARC, 1999) and Class D (not classifiable as to human carcinogenicity) (US EPA, 2001), respectively.

B. Regulatory Background

Methyl bromide is a Federal Hazardous Air Pollutant (HAP) and was identified as a Toxic Air Contaminant (TAC) in California in April 1993 under AB 2728. OEHHA has adopted an acute non-cancer Reference Exposure Level (REL) of 3900 µg/m^3 (1 ppm) and a chronic REL of 5 µg/m^3 (1 ppb) for methyl bromide (OEHHA, 1999a; OEHHA, 2001). Methyl bromide as a structural fumigant is listed under Proposition 65 as being known to cause developmental toxicity (OEHHA, 1999b).

VI. Conclusions

Methyl bromide is a neurotoxicant in both humans and animals. Neurotoxicity is a key toxicological endpoint for infants and children, primarily because of the prolonged period of development of the nervous system. Methyl bromide also induces developmental toxicity, another key toxicological endpoint for infants and children's health. Although there is concern for the toxicity of methyl bromide, exposures from stationary sources are not widespread and relatively low. Thus, OEHHA placed methyl bromide in Tier 2. Should evidence arise of significant exposures in the vicinity of stationary sources, OEHHA may revisit listing methyl bromide under SB 25.

VII. References

American Biogenics Corp. (1986). Two-generation reproduction study via inhalation in albino rats using methyl bromide. Study 450-1525.

Alexeeff GV, Kilgore WW. (1983) Methyl bromide. In: Residue Reviews. 88:102-153.

Anger WK, Moody L, Burg J, Brightwell WS, Taylor BJ, Russo JM, Dickerson N, Setzer JV, Johnson BL, Hicks K (1986). Neurobehavioral evaluation of soil and structural fumigators using methyl bromide and sulfuryl fluoride. Neurotoxicology 7(3):137-56.

Anger WK, Setzer JV, Russo JM, Brightwell WS, Wait RG, Johnson BL (1981). Neurobehavioral effects of methyl bromide inhalation exposures. Scand J Work Environ Health 7 Suppl 4:40-7.

Breslin WJ, Zablotny CL, Brabley GL, Lomax LG. (1990). Methyl bromide inhalation teratology study in New Zealand white rabbits (Parts I & II). Study No. K-000681-033. OTS Number 8EHQ-1189-0844 S. Toxicology Research Laboratory, Health and Environmental Sciences. Dow Chemical Company, Midland MI.

Busey WM (1993). Neuropathological evaluation of brains from F_0 and F_1 rats in a two-generation reproduction study with methyl bromide - pathology report. EPL project number 303-007.

Cal/EPA (1993) California Environmental Protection Agency. Letter to Carol Browner, Administrtor, U.S. EPA on methyl bromide uses in California. May, 1993.

Calvert GM, Mueller CA, Fajen JM, Chrislip DW, Russo J, Briggle T, Fleming LE, Suruda AJ, Steenland K (1998a). Health effects associated with sulfuryl fluoride and methyl bromide exposure among structural fumigation workers. Am J Public Health 88(12):1774-80.

Calvert GM, Talaska G, Mueller CA, Ammenheuser MM, Au WW, Fajen JM, Fleming LE, Briggle T, Ward E (1998b). Genotoxicity in workers exposed to methyl bromide. Mutat Res 417(2-3):115-28.

Garnier R, Rambourg-Schepens MO, Muller A, Hallier E (1996). Glutathione transferase activity and formation of macromolecular adducts in two cases of acute methyl bromide poisoning. Occup Environ Med 53(3):211-5.

Gotoh K, Nishizawa T, Yamaguchi T, Kanou H, Kasai T, Ohsawa M, Ohbayashi H, Aiso S, Ikawa N, Yamamoto S, Noguchi T, Nagano K, Enomoto M , Nozaki K, Sakabe H (1994). Two-year toxicological and carcinogenesis studies of methyl bromide in F344 rats and BDF1 mice. Proceedings of Second Asia-Pacific Symposium on Environmental and Occupational Health (22-24 July, 1993 in Kobe, Japan).

Hallier E, Langhof T, Dannappel D, Leutbecher M, Schroder K, Goergens HW, Muller A, Bolt HM (1993). Polymorphism of glutathione conjugation of methyl bromide, ethylene oxide and dichloromethane in human blood: influence on the induction of sister chromatid exchanges (SCE) in lymphocytes. Arch Toxicol 67(3):173-8.

Hardisty JF (1992). Histopathological evaluation of brains from rats - inhalation study of methyl bromide. EPL project number 303-007.

Hurtt ME, Morgan KT, Working PK (1987). Histopathology of acute toxic responses in selected tissues from rats exposed by inhalation to methyl bromide. Fundam Appl Toxicol 9(2):352-65.

Hurtt ME, Working PK (1988). Evaluation of spermatogenesis and sperm quality in the rat following acute inhalation exposure to methyl bromide. Fundam Appl Toxicol 10(3):490-8.

Hustinx WN, van de Laar RT, van Huffelen AC, Verwey JC, Meulenbelt J, Savelkoul TJ (1993). Systemic effects of inhalational methyl bromide poisoning: a study of nine cases occupationally exposed due to inadvertent spread during fumigation. Br J Ind Med 50(2):155-9.

IARC (1999). Methyl bromide. Re-evaluation of Some Organic Chemicals, Hydrazine and Hydrogen Peroxide. Vol. 71, Part 2. IARC Monographs on the Evaluation of Carcinogenic Risks to Humans. International Agency for Research on Cancer, Lyon, France: IARC, p. 721-35.

Kato N, Morinobu S, Ishizu S (1986). Subacute inhalation experiment for methyl bromide in rats. Ind Health 24(2):87-103.

NTP (1992). Toxicology and Carcinogenesis Studies of Methyl Bromide (CAS No. 74-83-9) in $B6C3F_1$ Mice (Inhalation Studies). NTP TR385. National Toxicology Program ,U.S. Department of Health and Human Services, Public Health Service, National Institutes of Health, Research Triangle Park NC.

OEHHA (1999a). Air Toxics Hot Spots Program Risk Assessment Guidelines. Part I. The Determination of Acute Reference Exposure Levels for Airborne Toxicants. Office of Environmental Health Hazard Assessment, California Environmental Protection Agency, Oakland CA.

OEHHA (1999b). Safe Drinking Water And Toxic Enforcement Act Of 1986. Chemicals Known To The State To Cause Cancer Or Reproductive Toxicity. Office of Environmental Health Hazard Assessment, Reproductive and Cancer Hazard Assessment Section, Oakland, CA.

OEHHA (2001). Air Toxics Hot Spots Program Risk Assessment Guidelines. Part III. Technical Support Document for the Determination of Noncancer Chronic Reference Exposure Levels for Airborne Toxicants. Office of Environmental Health Hazard Assessment, California Environmental Protection Agency, Oakland CA.

Reuzel PG, Dreef-van der Meulen HC, Hollanders VM, Kuper CF, Feron VJ, van der Heijden CA (1991). Chronic inhalation toxicity and carcinogenicity study of methyl bromide in Wistar rats. Food Chem Toxicol 29(1):31-9.

Sikov MR, Cannon WC, Carr DB, Miller RA, Montgomery LF, Phelps DW (Batelle Pacific Northwest Lab) (1981). Teratological assessment of butylene. Contract no. 210-78-0025. Division of Biomedical and Behavioural Science, National Institute for Occupational Safety and Health, U.S. Department of Health and Human Services.

US EPA (2001). United States Environmental Protection Agency, Integrated Risk Information System (IRIS)(Internet version): Methyl bromide. Office of Research and Development, National Center for Environmental Assessment, Washington DC.

Watrous RM (1942). Methyl bromide. Ind Med 11(12):575-9.